

Medical Marijuana and Epilepsy

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CONTENT HIGHLIGHTS

- Medical marijuana is the whole plant of marijuana used for medical purposes. Cannabinoids refer to substances in cannabis that act on cells in the body to cause some effect.
- The two major ingredients in cannabinoids are: tetrahydrocannabinol (THC) and cannabidiol (CBD).
- There is evidence that cannabis can be helpful in controlling seizures, especially for difficult to control conditions like Lennox-Gastaut syndrome (LGS) in children and adults and Dravet syndrome in children.
- Marijuana or cannabis has a number of side effects. In open-labeled studies on the use of cannabidiol, side effects included sleepiness, diarrhea, fatigue, and decreased appetite. CBD also has interactions with some epilepsy medications.
- A number of states in the United States have laws allowing cannabis to be recommended and dispensed to people for medical reasons.

What to do about the medical use of marijuana (cannabis) as a potential treatment for a number of neurological conditions, including epilepsy, is of much debate. There are legal issues surrounding access to cannabis, as well as some scientific research on the usefulness and safety of marijuana as a treatment for seizures. Additionally, many different substances containing cannabis are being used, making it difficult to study.

What is medical marijuana or cannabis?

Marijuana is known by many names; the most common is cannabis. This is the Latin name used most often by botanists and pharmaceutical companies. The word *marijuana* usually refers to the leaves and female flowers of the cannabis plant. Medical marijuana is whole plant marijuana used for medical purposes.

Cannabinoids are substances in cannabis that act on cells in the body (called cannabinoid receptors) to cause some effect. Two major ingredients include:

- Tetrahydrocannabinol, or THC, which causes the psychoactive effects of "getting high"
- Cannabidiol, or CBD, which does not cause psychoactive effects but has shown some positive effects on certain body systems and may potentially affect seizures

Glossary Of Cannabinoid Terms

GW Pharmaceuticals, Plc., has shared a glossary to aid readers' understanding of cannabis, marijuana, and related terms.

Does cannabis help seizures?

Evidence from laboratory studies, anecdotal reports, and small clinical studies from a number of years ago suggest that cannabidiol, a non-psychoactive compound of cannabis, could potentially be helpful in controlling seizures. Conducting studies can be difficult as researchers have limited access to marijuana due to federal regulations and even more limited access to cannabidiol; there are also increased financial and time constraints.

Cannabidiol (CBD)

Open-label studies in the U.S. of Epidiolex (a drug derived from cannabidiol or CBD) are being performed. Epidiolex is a purified, 99% oil-based CBD extract from the cannabis plant and is produced by GW Pharmaceuticals to give known and consistent amounts in each dose. The U.S. Food and Drug Administration (FDA) has given some epilepsy centers permission to use this drug as "compassionate use" for a limited number of people at each center.

Recently, gold-standard studies (double-blind, placebo-controlled studies) have finished for difficult epilepsies such as Lennox-Gastaut syndrome (LGS) in children and adults and Dravet syndrome in children. Information from these studies has been presented at major scientific meetings and in press releases by GW Pharmaceuticals.

Results from 214 people who received Epidiolex (99% CBD) in an open-label study (without a placebo control) and who completed 12 weeks or more on the drug were published in *Lancet Neurology*¹.

- People who received Epidiolex ranged from 2 to 26 years old with an average age of 11.
- All had epilepsy that did not respond to currently available treatments.
- During the study, seizures decreased by an average of 54%.

- People taking the anti-seizure medication clobazam (Onfi) seemed to have a better response when compared to those that were not on this medication.

In addition, two gold-standard studies using Epidiolex for LGS in children and adults and one with children who have Dravet syndrome showed promising results.

- Drop seizures were reduced in the two LGS studies by over 40% compared to less than 20% for people who got the placebo, which was statistically significant.
- In the Dravet study, approximately 40% reduction in convulsive seizures was noted compared to 17% reduction for the placebo group. Again, significance was found compared to the placebo group.

Other studies using Epidiolex in people with Tuberous Sclerosis are ongoing as well.

An Israeli study² using a product that had 20 parts of CBD to 1 part of THC was performed in an open-label format for children up to age 18 years with hard to control epilepsy. A significant number of people reported seizure reduction with 7% stating seizures worsened.

Does cannabis have side effects?

Marijuana or cannabis in general has a number of effects depending on how it is ingested. For example, if smoked, the risk factors associated with smoking apply to marijuana.

Side effects of the preparations used to treat seizures have not been well documented in anecdotal reports as varying doses and strains have been used. Increased appetite and memory problems have been reported.

It is important that people know that even though marijuana is a plant, it is broken down in a person's liver like many medicines. There is some misbelief that because it is a plant or oil from a plant, in the case of CBD, that marijuana is completely safe. However, medication interactions can occur that need further study.

Cannabidiol (CBD)

The open-labeled study discussed above included safety data from 214 people.

- Side effects that occurred in 10% or more of people included
 - sleepiness (21%)
 - diarrhea (17%)

- fatigue (17%)
- decreased appetite (16%)
- Most side effects were described as mild or moderate and went away.
- Serious side effects happened in 52 people
 - 22 of these were possibly related to the drug
 - The most common serious possible side effect was status epilepticus, when a person has long or repeated seizures.

The safety data from the trials in people with Lennox Gastaut syndrome and Dravet syndrome has shown similar side effects in that tiredness, diarrhea, and upset stomach feeling are reported the most.

Interestingly, people getting the placebo report lots of diarrhea and upset stomach feeling as well. This may be due to both products being oil.

There are some interesting drug-to-drug interactions that are starting to come forward with these studies of CBD in epilepsy syndromes.

- It appears that people who had increases in their liver enzymes to a level three times or more than normal were also on valproic acid (VPA), a commonly used anti-seizure medication. The levels of VPA were not increased when taken with CBD. Therefore, it is thought that as VPA is broken down, one of its parts may interact with CBD, thus putting some people at increased risk for liver issues.
- Also, as clobazam (Onfi) is broken down, its major part appears to interact with CBD in some people and may be the cause of tiredness that is seen with some people who are on CBD and Onfi.
- More work in this area is needed to fully understand these drug to drug interactions.

What are the laws governing medical marijuana?

A number of states in the U.S. have laws allowing cannabis to be recommended and dispensed to people for medical reasons. However, this does conflict with federal laws and there are further complications for research on cannabis due to federal restrictions. This can mean physicians who choose to follow the state laws on medical use of marijuana could be breaking a federal law.

Some states have acted to include protections for physicians, but they must be aware of both federal and state laws and the potential implications. A clearer understanding of the laws governing this issue is needed.

It is also illegal for parents to carry medical cannabis across state lines or have products shipped to them. Companies will often label CBD products as hemp extract to skirt laws. However, if the product has CBD in it, then it is a Schedule I substance and it is illegal to ship it across state lines.

Should a person with epilepsy pursue medical cannabis if all other medications do not work?

When conventional treatments do not work, as is the case for roughly 30% of people with epilepsy, it is not unreasonable to consider cannabis. This is why some states have approved it for “compassionate access.” However, this should only be considered after a thorough evaluation at a specialized epilepsy center and once conventional treatments (pharmacologic and nonpharmacologic) have been reasonably tried.

The Epilepsy Foundation urges anyone exploring any treatment for their epilepsy, as permitted under their state law, to work with their treating physician to make the best decisions for their own care.

What is the position of the Epilepsy Foundation on cannabis³?

Learn more about the Epilepsy Foundation's state and federal advocacy efforts on removing barriers to cannabis research and supporting access to medical cannabis (marijuana) in consultation with the treating physician. Also find a statement on the Foundation's position on lifting barriers to cannabis, increasing research, and improving safe, legal access for intractable epilepsy.

References

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3. Gattone PM, Lammert W, and Devinsky O. Epilepsy Foundation of America Position Statement Medical Marijuana in Epilepsy [online].
4. Devinsky O, Cilio MR, Cross H, et al. Cannabidiol: pharmacology and potential therapeutic role in epilepsy and other neuropsychiatric disorders. *Epilepsia* 2014.

